

Please add new claims 64-69 as follows:

64. (new) The anticode oligomer of Claim 54, 55 or 56, wherein said anticode oligomer contains at least one phosphorothioate-modified nucleotide.

65. (new) The anticode oligomer of Claim 64; and a pharmaceutically acceptable carrier.

66. (new) The anticode oligomer of Claim 64, wherein said anticode oligomer is a phosphodiester/phosphorothioate chimera.  
*E 10*

67. (new) The anticode oligomer of Claim 66 wherein the oligonucleotide comprises at least 2 to 3 phosphorothioate linkages. *F*

68. (new) The anticode oligomer of Claim 66 or 67; and a pharmaceutically acceptable carrier.

69. (new) The anticode oligomer of Claim 54, 55 or 56, wherein said anticode oligomer contains at least one phosphoramidate-modified nucleotide.

#### REMARKS

Applicants note with appreciation that Claims 53-63 have been found to be free of the prior art. Claims 53-63 were pending in this application. Claims 53-56, 58 and 63 have been amended without prejudice to Applicant's right to pursue the canceled subject matter in subsequent applications, and added new claims 64-69. Accordingly, claims 53-69 will be pending upon entry of this amendment. Claims 53-69 are fully supported by the specification

as originally filed, such that the above-made amendments do not constitute new matter under 35 U.S.C. § 132.

Applicants have amended the specification to correct duplication of related application information as pointed out by the Examiner. Applicants have also added sequence identifiers to the brief description of the drawings as requested by the Examiner. A marked up version of the amended paragraphs in the specification, with amendments indicated by bracketing for deletions and underlining for additions, is attached hereto as Exhibit A. No new matter has been added by these amendments.

Applicants have hereinabove amended claims 53-56, 58 and 63 to more particularly point out and distinctly claim the subject matter of the instant invention. A marked up version of the amended claims, with amendments indicated by bracketing for deletions and underlining for additions, is attached hereto as Exhibit B.

**The Rejections Under 35 U.S.C. § 112 Should Be Withdrawn**

Claims 53 and 55 stand rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite. Claims 53 and 55 have been amended, as suggested by the Examiner in the June 20, 2001 Office Action (at page 3), to more particularly point out and distinctly claim the subject matter which the Applicants regard as the invention, in accordance with the requirements under 35 U.S.C. §112. As such, Applicants respectfully submit that the rejections of claims 53 and 55 under 35 U.S.C. §112, second paragraph have been obviated and overcome, and therefore Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph be withdrawn.

Claims 54-63 stand rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter not described in the specification to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. Claims 53-56, 58

and 63 have been amended to specifically recite anticode oligomers to human bcl-2, which as the Examiner acknowledges in the present Office Action at page 3, the originally filed specification clearly teaches. As such, Applicants respectfully submit that the rejections of claims 54-63 under 35 U.S.C. §112, first paragraph have been obviated and overcome, and therefore Applicants respectfully request that the rejections under 35 U.S.C. §112, first paragraph be withdrawn.

**The Rejections Based on Non-Statutory Double Patenting**

Claims 53-63 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-41 of U.S. Patent No. 5,831,066. Further, Claims 53-63 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,040,181. Applicants will consider submitting a terminal disclaimer in connection with the instant application upon the finding of allowable subject matter by the Examiner.

**CONCLUSION**

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that each ground for rejection or objection has been overcome or obviated, and that all of the pending claims are in

condition for allowance. Withdrawal of all outstanding rejections and objections is therefore respectfully requested. An early allowance is earnestly sought.

Respectfully submitted,

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Enclosures

## EXHIBIT A

### Marked up version of replacement paragraphs

On page 1, line 1, replace the paragraph beginning "This application is a" with the following paragraph:

This application is a continuation of Application [Serial] No. 09/080,285, filed [on] May 18, 1998 and issued as U.S. Patent No. 6,040,181 on March 21, 2000, which is a continuation of Application [Serial] No. 08/465,485, filed [on] June 5, 1995 and issued as U.S. Patent No. 5,831,066 on November 3, 1998, which is a continuation of Application [Serial] No. 08/124,256 filed September 20, 1993, abandoned, which is a continuation-in-part of Application [Serial] No. 07/840,716, filed February 21, 1992, abandoned, which is a continuation-in-part of Application No. 07/288,692, filed December 22, 1988, abandoned.

On page 8, line 4, replace the paragraph beginning "Figure 13" with the following paragraph:

Figure 13 shows optimization of antisense bcl-2 oligomer sequences using the oligonucleotides 5'-TCTCCCAGCGTGCGCCAT-3' (SEQ ID NO:17), 5'-TGCACTCACGCTCGGCCT-3' (SEQ ID NO:18), 5'-GCGCGGCCGGCGGGCA-3' (SEQ ID NO:26), 5'-GGGCGGAGGCCGGCGG-3' (SEQ ID NO:27), 5'-AGCGGCCGGCGGCAGCGC-3' (SEQ ID NO:28) and 5'-GGGCCGGGAAGGGCGCCCGC-3' (SEQ ID NO:29).

**EXHIBIT B**

**Marked up version of amended claims**

53. (amended) An anticode oligomer complementary to bcl-2 mRNA consisting of from [10-35] 18-35 bases and comprising the nucleotide sequence TCTCCCAGCGTGCGCCAT (SEQ ID NO:17).

54. (amended) An anticode oligomer, wherein said anticode oligomer is an antisense oligonucleotide complementary to a portion of the pre-mRNA encoding the human bcl-2 gene.

55. (amended) The anticode oligomer of Claim 54, wherein said anticode oligomer is an antisense oligonucleotide complementary to a portion of the region of [the] a splice acceptor site or splice donor site of the pre-mRNA encoding the human bcl-2 gene.

56. (amended) An anticode oligomer, wherein said anticode oligomer is an antisense oligonucleotide complementary to a portion of the 5'-untranslated region of the human bcl-2 mRNA.

58. (amended) The anticode oligomer of Claim 53, [54, 55 or 56,] wherein said anticode oligomer contains at least one phosphorothioate-modified nucleotide and is complementary to a portion of the pre-mRNA or mRNA encoding the human bcl-2 gene.

63. (amended) The anticode oligomer of Claim 53, [54, 55 or 56,] wherein said anticode oligomer contains at least one phosphoramidate-modified nucleotide and is complementary to a portion of the pre-mRNA or mRNA encoding the human bcl-2 gene.

**EXHIBIT C**

**Claims pending in Serial No. 09/375,514**

53. (amended) An anticode oligomer complementary to bcl-2 mRNA consisting of from 18-35 bases and comprising the nucleotide sequence TCTCCCAGCGTGCGCCAT (SEQ ID NO:17).

54. (amended) An anticode oligomer, wherein said anticode oligomer is an antisense oligonucleotide complementary to a portion of the pre-mRNA encoding the human bcl-2 gene.

55. (amended) The anticode oligomer of Claim 54, wherein said anticode oligomer is an antisense oligonucleotide complementary to a portion of the region of a splice acceptor site or splice donor site of the pre-mRNA encoding the human bcl-2 gene.

56. (amended) An anticode oligomer, wherein said anticode oligomer is an antisense oligonucleotide complementary to a portion of the 5'-untranslated region of the human bcl-2 mRNA.

57. The anticode oligomer of Claim 53, 54, 55 or 56; and a pharmaceutically acceptable carrier.

58. (amended) The anticode oligomer of Claim 53, wherein said anticode oligomer contains at least one phosphorothioate-modified nucleotide and is complementary to a portion of the pre-mRNA or mRNA encoding the human bcl-2 gene.

59. The anticode oligomer of Claim 58; and a pharmaceutically acceptable carrier.

60. The anticode oligomer of Claim 58, wherein said anticode oligomer is a

phosphodiester/phosphorothioate chimera.

61. The anticode oligomer of Claim 60 wherein the oligonucleotide comprises at least 2 to 3 phosphorothioate linkages.

62. The anticode oligomer of Claim 60 or 61; and a pharmaceutically acceptable carrier.

63. (amended) The anticode oligomer of Claim 53, wherein said anticode oligomer contains at least one phosphoramidate-modified nucleotide and is complementary to a portion of the pre-mRNA or mRNA encoding the human bcl-2 gene.

64. (new) The anticode oligomer of Claim 54, 55 or 56, wherein said anticode oligomer contains at least one phosphorothioate-modified nucleotide.

65. (new) The anticode oligomer of Claim 64; and a pharmaceutically acceptable carrier.

66. (new) The anticode oligomer of Claim 64, wherein said anticode oligomer is a phosphodiester/phosphorothioate chimera.

67. (new) The anticode oligomer of Claim 66 wherein the oligonucleotide comprises at least 2 to 3 phosphorothioate linkages.

68. (new) The anticode oligomer of Claim 66 or 67; and a pharmaceutically acceptable carrier.

69. (new) The anticode oligomer of Claim 54, 55 or 56, wherein said anticode oligomer contains at least one phosphoramidate-modified nucleotide.